UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/595,200	03/22/2006	Se Hwan Yang	58049-00025	4449

35736 7590 06/26/2008

JHK LAW
P.O. BOX 1078
LA CANADA, CA 91012-1078

EXAMINER	
WANG, CHANG YU	
ART UNIT	PAPER NUMBER
1649	
MAIL DATE	DELIVERY MODE
06/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/595,200	YANG ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/22/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/22/06* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/22/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Election/Restrictions

1. Claims 1-16 are pending and under examination in this office action.

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

3. The drawings/figures are objected to because sequence listings included in the specification must not be duplicated in the drawings. See 37 C.F.R. §1.58(a) and §1.83. Appropriate correction is required.

Specification

4. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.

(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Claim Objections

5. Claims 1, 12, 14 and 15 are objected to because of the following informalities: the claims recite "a gene coding human FSH". However, the common use for the recitation should be "a gene encoding human FSH". Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 10 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ novel biological materials, specifically the expression vector RC/CMV-dhfr-TPL-hFSH beta/alpha as recited in claim 7 and a recombinant transformant DPFC325 deposited as Accession No. KCLRF-BP-00082 as recited in claims 10 and 16. Since the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the biological materials are not so obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological materials. The specification does not disclose a repeatable process to obtain the biological materials and it is not apparent if the biological materials are readily available to the public. It is noted that Applicant only has deposited the biological material DPFC325 (p. 28 of the specification), but there is no indication in the specification as to public availability. If the deposit is made under the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty and that the biological materials will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, Applicant may

provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit will be made (see 37 C.F.R. § 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Applicant's attention is directed to M.P.E.P. §2400 in general, and specifically to §2411.05, as well as to 37 C.F.R. § 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." The specification should be amended to include this information, however, Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information. Finally, Applicant is advised that the address for the ATCC has changed, and that the new address should appear in the specification. The new address is:

American Type Culture Collection

10801 University Boulevard

Manassas, VA 20110-2209

6. Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 1-16 are drawn to an expression vector, a host cell containing the expression vector and the method of making hFSH. The claims encompass a genus of DNA sequences coding human FSH, a genus of a promoter sequence, a genus of a polyadenylation motif sequence, and a genus of DNA sequences for dihydrofolate reductase (DHFR) gene. Applicant has not disclosed sufficient species for the broad genus of DNA sequences coding human FSH gene, and for the broad genus of DNA sequences for dihydrofolate reductase (DHFR) gene. The specification only describes SEQ ID NO:1 and SEQ ID NO:2 for human FSH alpha and beta subunits and only

describes SEQ ID NO:12 for DHFR gene. However, the claims are not limited to the sequences as set forth above.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant is in possession of and what Applicant is claiming. From the specification, it is clear that Applicant is in possession of SEQ ID NO:1-2 for human FSH alpha and beta subunits and also in possession of SEQ ID NO:12 for DHFR. Applicant is also predictably in possession of a promoter sequence and a polyadenylation motif sequence since these sequences are well known in the art. However, Applicant is not in possession other hFSH sequences or other DHFR sequences that can be used in the claimed expression vector. The specification only describes SEQ ID NO:1 and SEQ ID NO:2 for human FSH alpha and beta subunits and only describes SEQ ID NO:12 for DHFR gene. There is no identification of any particular portion of the structure that must be conserved. The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of human FSH sequences and DHFR sequences. There is no description of the conserved regions which are critical to the function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure of other human FSH sequences to SEQ ID NOs:1-2 function and that of other DHFR sequences to SEQ ID NO:12 function. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify other

sequences for human FSH and DHFR might be. Since the common characteristics/features of other human FSH and DHFR sequences are unknown, a skilled artisan cannot envision the functional correlations of the genus with the claimed invention. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the genus of proteins.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to

be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, an expression vector comprising a gene coding human FSH, a promoter sequence, a polyadenylation motif sequence, and a DHFR gene, a transformant comprising the claimed expression vector and the method of making human FSH using the claimed transformant have not met the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement. See MPEP § 2163.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is indefinite because the term "RC/CMV-dhfr-TPL-hFSH beta/alpha" recited in the claims without a reference to a precise amino acid sequence identified by a proper SEQ ID NO. Without identification of property or combination of properties which are unique to and, therefore, definitive of the instant recitations, the metes and bounds of the claims remain undetermined. Further, the use of laboratory designations

only to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. The rejection can be obviated by amending the claims to specifically and uniquely identify RC/CMV-dhfr-TPL-hFSH beta/alpha, for example, by SEQ ID NO.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 8-9, and 11-15 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,674,711 as evidenced by US 6,632,637.

Claims 1, 5, 8-9, and 11-15 are drawn to an expression vector, a transformant comprising the claimed expression vector and a method of making human FSH protein using the expression vector wherein the expression vector comprises a gene coding human FSH, a promoter sequence, a polyadenylation motif sequence and a DHFR gene.

US 5,674,711 (the '711 patent) teaches an expression vector comprising a gene coding human FSH alpha or beta, a promoter sequence, a polyadenylation (polyA) motif sequence and a dihydrofolate reductase (DHFR) gene as recited in instant claims 1 and 5-6 (see cols. 3-13; figure 4; examples 1-6, in particular). The '711 patent teaches an expression vector containing a DNA sequence encoding human FSH alpha subunit, a

mouse metallothionein-I (MT-1) promoter, a SV40 early polyA motif and a mouse DHFR gene (see col.3, line 25-col.4, line 31; examples 1-6, in particular) in an expression vector CLH3AXSV2, which meets the limitations as recited in instant claims 1 and 5-6 (see col.3, line 25-col.4, line 31, in particular). The '711 patent teaches that a polyA motif sequence prevents mRNA degradation (see col.2, lines 12-16, in particular). The '711 patent teaches that FSH functions as a dimer containing FSH alpha and beta subunits (see col.1, lines 33-65, in particular). The '711 patent also teaches co-expression human FSH alpha and beta subunits by co-transfecting an expression vector containing a FSH alpha subunit gene and an expression vector containing a FSH beta subunit gene in CHO/DHFR- cells (see cols. 2-4, examples 1-2; col.14-16, claims 1-16, in particular).

The '711 patent also teaches a transformant comprising the claimed vector of claims 1 and 5-6 as recited in instant claims 8-9 (see col.4, line 32-col.6, line 21, in particular). The '711 patent also teaches a host cell is a CHO originated cell line (CHO/dhfr-) harboring damaged DHFR gene as recited in instant claims 13 and 15 (see col.4, line 32-col.6, line 21; examples 1-3, in particular). In addition, the '711 patent teaches a method of making human FSH protein as recited in instant claims 11-15 (see col.4, line 32-col.6, line 21; examples 1-6, in particular).

Although the '711 patent does not explicitly teach SEQ ID NO:13 as a polyA motif sequence as recited in instant claim 5, the sequence of a polyA motif in the early gene of SV40 virus is known in the art as evidenced by US 6,632,637 (see the sequence

search results and alignment below). Thus, claims 1, 5, 8-9, and 11-15 are anticipated by US 5,674,711.

The sequence search results disclose as follows:

SEQ ID NO:12

```
US-09-175-690A-1
; Sequence 1, Application US/09175690A
; Patent No. 6136536
;  GENERAL INFORMATION:
;    APPLICANT:  Tomkinson, Kathleen et al
;    TITLE OF INVENTION:  RAPID GENERATION OF STABLE MAMMALIAN
;    TITLE OF INVENTION:  CELL LINES PRODUCING HIGH LEVELS OF RECOMBINANT PROTEINS
;    NUMBER OF SEQUENCES:  1
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  GENETICS INSTITUTE, INC.
;      STREET:  87 CAMBRIDGEPARK DRIVE
;      CITY:  CAMBRIDGE,
;      STATE:  MASSACHUSETTS
;      COUNTRY:  US
;      ZIP:  02140
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.30
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/09/175,690A
;      FILING DATE:  10-DEC-1998
;      CLASSIFICATION:  435
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  LAZAR, STEVEN R.
;      REGISTRATION NUMBER:  32,618
;      REFERENCE/DOCKET NUMBER:  GI 5310A
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (617) 498-8260
;      TELEFAX:  (617) 876-5851
;  INFORMATION FOR SEQ ID NO:  1:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  5639 base pairs
;      TYPE:  nucleic acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  DNA (genomic)
US-09-175-690A-1

  Query Match           100.0%;  Score 564;  DB 3;  Length 5639;
  Best Local Similarity   100.0%;  Pred. No. 8.9e-180;
  Matches  564;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 ATGGTTCGACCATTGAACTGCATCGTCGCCGTGTCCCAAAATATGGGGATTGGCAAGAAC 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1935 ATGGTTCGACCATTGAACTGCATCGTCGCCGTGTCCCAAAATATGGGGATTGGCAAGAAC 1994

Qy         61 GGAGACCTACCCTGGCCTCCGCTCAGGAACGAGTTCAAGTACTTCCAAAGAATGACCACA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1995 GGAGACCTACCCTGGCCTCCGCTCAGGAACGAGTTCAAGTACTTCCAAAGAATGACCACA 2054

Qy        121 ACCTCTTCAGTGGAAGGTAAACAGAATCTGGTGATTATGGGTAGGAAAACCTGGTTCTCC 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2055 ACCTCTTCAGTGGAAGGTAAACAGAATCTGGTGATTATGGGTAGGAAAACCTGGTTCTCC 2114

Qy        181 ATTCCTGAGAAGAATCGACCTTTAAAGGACAGAATTAATATAGTTCTCAGTAGAGAACTC 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2115 ATTCCTGAGAAGAATCGACCTTTAAAGGACAGAATTAATATAGTTCTCAGTAGAGAACTC 2174

Qy        241 AAAGAACCACCACGAGGAGCTCATTTTCTTGCCAAAAGTTTGGATGATGCCTTAAGACTT 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2175 AAAGAACCACCACGAGGAGCTCATTTTCTTGCCAAAAGTTTGGATGATGCCTTAAGACTT 2234

Qy        301 ATTGAACAACCGGAATTGGCAAGTAAAGTAGACATGGTTTGGATATGCGGAGGCAGTTCT 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2235 ATTGAACAACCGGAATTGGCAAGTAAAGTAGACATGGTTTGGATATGCGGAGGCAGTTCT 2294

Qy        361 GTTTACCAGGAAGCCATGAATCAACCAGGCCACCTCAGACTCTTTGTGACAAGGATCATG 420
```

```
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2295 GTTTACCAGGAAGCCATGAATCAACCAGGCCACCICAGACTCTTTCTGACAAGGATCATG 2354

Qy        421 CAGGAATTTGAAAGTGACACCTTTTTCCCAGAAATTGATTTGGGGAAATATAAACTTCTC 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2355 CAGGAATTTGAAAGTGACACCTTTTTCCCAGAAATTGATTTGGGGAAATATAAACTTCTC 2414

Qy        481 CCAGAATACCCAGCGGTCCTCTCTGAGGTCCAGGAGGAAAAAGGCATCAAGTATAAGTTT 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2415 CCAGAATACCCAGCGGTCCTCTCTGAGGTCCAGGAGGAAAAAGGCATCAAGTATAAGTTT 2474

Qy        541 GAAGTCTACGAGAAGAAAGACTAA 564
              ||||||||||||||||||||||||
Db       2475 GAAGTCTACGAGAAGAAAGACTAA 2498
```

SEQ ID NO:13

```
US-09-687-050-1/c
; Sequence 1, Application US/09687050
; Patent No. 6672637
; GENERAL INFORMATION:
;  APPLICANT:  McGrew, Jeffrey T.
;  TITLE OF INVENTION:  VECTORS AND METHODS FOR RECOMBINANT PROTEIN EXPRESSION
;  FILE REFERENCE:  2902-A
;  CURRENT APPLICATION NUMBER: US/09/687,050
;  CURRENT FILING DATE:  2000-10-12
;  PRIOR APPLICATION NUMBER:  60/159,177
;  PRIOR FILING DATE:  1999-10-13
;  NUMBER OF SEQ ID NOS:  10
;  SOFTWARE:  PatentIn version 3.0
; SEQ ID NO 1
;  LENGTH: 222
;  TYPE: DNA
;  ORGANISM: SV40
US-09-687-050-1

  Query Match             100.0%;  Score 130;  DB 3;  Length 222;
  Best Local Similarity   100.0%;  Pred. No. 6.2e-25;
  Matches  130;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 AACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTTCACA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        134 AACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTTCACA 75

Qy         61 AATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAAACTCATCAATGTATCT 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         74 AATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAAACTCATCAATGTATCT 15

Qy        121 TATCATGTCT 130
              ||||||||||
Db         14 TATCATGTCT 5
```

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 5-6, 8-9 and 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,674,711 in view of US2003144189, US 6,632,637, US 6,136,536, US20030083242, and US 6,852,510.

Claims 1-3, 5-6, 8-9 and 11-15 are drawn to an expression vector, a transformant and a method of making human FSH protein wherein the expression vector comprises a gene coding human FSH (SEQ ID NOs 1-2 in claim 2), a promoter sequence (SEQ ID NO:8 in claim 3), a polyadenylation motif sequence (SEQ ID NO:13 for SV40 polyA, SEQ ID NO:14 for BGH in claim 5) and a DHFR gene (SEQ ID NO:12 in claim 6) and optionally comprises IRES (SEQ ID NO:7 in claim 2).

US 5,674,711 (the '711 patent) is as set forth above at paragraph 8 but fails to teach SEQ ID NOs: 1 & 2 for human FSH (claim 2) and fails to teach SEQ ID NO: 12 for a DHFR gene (claim 6). The '711 patent also fails to teach an expression vector containing internal ribosomal entry site (IRES) for expressing multiple genes and fails to teach SEQ ID NO:7 as an IRES sequence (claim 2), SEQ ID NO:8 for a promoter sequence of early gene of CMV (claim 3).

The human FSH protein generated from these different sequences as recited in instant claims 1-3 and 5-6 would be considered as a product-by-process because the structure and activity of FSH generated from these different nucleotide sequences are identical to that of the '711 patent.

SEQ ID NOs:1 & 2 for human FSH alpha and beta subunits (claim 2) and SEQ ID NO:12 for a DHFR gene (claim 6):

Although the '711 patent does not explicitly teaches SEQ ID NOs:1 & 2 encoding human FSH alpha and beta subunits respectively, US2003144189 teaches the amino acid sequences of human FSH alpha and beta subunits. US2003144189 teaches a DNA sequence encoding human FSH alpha subunit and having 99.5% identity to instant SEQ ID NO:1 as recited in instant claim 2 (see sequence alignment below). Although the DNA sequence of US2003144189 has one nucleic acid mismatch to the instant SEQ ID NO:1, the translated amino acid sequence human of US2003144189 is identical to the amino acid sequence encoded by instant SEQ ID NO:1 based on the "translate tool" on the ExPASy website (http://ca.expasy.org/tools/dna.html).

In addition, although the '711 patent does not explicitly teach SEQ ID NO:2 encoding human FSH beta subunit, US2003144189 teaches a DNA sequence encoding human FSH alpha and having 98.8% identity to instant SEQ ID NO:2 (see sequence alignment below). Although there is one-amino acid mismatch (i.e. a three-nucleotide mismatch) between the amino acid sequence of the instant human FSH beta subunit and that of US2003144189, the FSH of the instant application is expected to work as

that in US2003144189 because it is known in the art that cysteine and valine residues are conserved amino acids, which would not change the activity of FSH.

Furthermore, although the '711 patent does not explicitly teach SEQ ID NO:12 as a sequence for a DHFR gene as recited in instant claim 6, US 6,136,536 teaches the DNA sequence of DHFR (see the sequence alignment below).

SEQ ID No:7 for IRES, SEQ ID NO: 7 for a CMV promoter, SEQ ID NO:13 for a SV40 polyA motif, SEQ ID NO: 14 for a BGH polyA motif (claims 2-3 and 5):

Although the '711 patent does not teach an IRES sequence in an expression vector, US Patent No. 6,632,637 (the '637 patent) teaches an expression vector that can express at least two exogenous genes wherein the two exogenous genes are separated by an internal ribosomal entry site (col.1, line 38-col.2, line 63). The '637 patent teach an expression vector containing an a CMV promoter, an IL4R gene, an IRES, a DHFR gene and a SV40 polyA sequence and a polyA sequence of BGH as recited in claims 1-3 and 5-6 (see figure 1; col.2, line 13-col.6. line 35; col.6 table1; col. 29-32, claims 1-44, in particular). The '637 patent also teaches a transformant of DHFR-CHO cell line containing an expression vector comprising an a CMV promoter, an IL4R gene, an IRES, a DHFR gene and a SV40 polyA sequence and a polyA sequence of BGH as recited in instant claims 8-9 and also teaches a method of making protein as recited in instant claims 11-15 (see col.7, line 1-col.9, line 55, in particular). The '637 patent teaches a DNA sequence of SV40 polyA motif having 100% identity to SEQ ID NO:13 and a DNA sequence of the polyA motif sequence of BGH gene having 100%

identity to SEQ ID NO:14 as recited in instant claim 5 (see sequence alignment below and at paragraph 8; cols. 5-6, in particular).

Although the '637 patent does not explicitly teach a DNA sequence for IRES of the instant SEQ ID NO:7 as recited in instant claim 2, US patent No. 6,852,510 (the '510 patent) teaches the DNA sequence of IRES (see sequence alignment below). The '510 patent teaches an expression vector that can express at least two exogenous genes wherein the two exogenous genes are separated by an internal ribosomal entry site (IRES) (see col.2, lines 36-50, in particular). The '510 patent teaches a DNA sequence of IRES having a DNA sequence 97% identical to instant SEQ ID NO:7 (see sequence search results and alignment below). Although the N-terminus of the IRES DNA sequence of the '510 patent is different from that of the instant SEQ ID NO:7 with a 10-nucleotide mismatch, these 10 nucleotides are for different restriction enzyme sites and are not essential for ribosomal entry because both the instant SEQ ID NO:7 and the DNA sequence of IRES in the '510 patent have the same function for internal ribosomal entry. Thus, the instant SEQ ID NO:7 for IRES is expected to work as that of IRES in the '637 patent or the '510 patent.

In addition, the '637 patent and the '510 patent teach an expression vector containing a CMV promoter as recited in instant claim 3 (see col.5, lines 16-30 in the '637 patent; also see col.2, lines 36-50 in the 510 patent, in particular). Although the '637 and '510 patent do not explicitly teach the DNA sequence of a CMV promoter, US20030083242 teaches a CMV promoter having a DNA sequence 99.3% identical to instant SEQ ID NO:8 (see sequence alignment below). Although the CMV promoter

sequence has a 3-nucleotide mismatch to instant SEQ ID NO:8 at the C-terminus, which is not essential because both of the CMV sequence have the same function to serve as a promoter. Thus, the instant SEQ ID NO:8 is expected to work as that of the '637 patent , the '510 patent or US20030083242.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to use an expression vector of the '637 patent that contains a CMV promoter, an IRES, a DHFR gene, a SV40 polyA sequence and a BGH polyA sequence to express both human FSH alpha and beta subunits in one vector as recited in the instant claim 2 to generate human FSH of the '711 patent. The person of ordinary skill in the art would have been motivated to do so with an expectation of success because the expression vector of the '637 patent has successfully been used to express two exogenous genes in one expression vector in CHO/dhfr- cells. Thus, the instant expression vector comprising SEQ ID NOs:1-2 for human FSH alpha and beta, SEQ ID NO:7 for an IRES, SEQ ID NO:8 for a CMV promoter, SEQ ID NO:13 for a SV40 polyA sequence, SEQ ID NO:14 for a BGH polyA sequence and SEQ ID NO:12 for DHFR is expected to work to generate a human FSH dimer containing both FSH alpha and beta subunits in CHO/dhfr- cells. Thus, the claimed vector, transformant and method of making proteins are obvious over the applied references as set forth above.

Note that

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980); see also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) and *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992). See MPEP § 2144.06.

"The selection of a known material based on its suitability for its intended use supported a prima facie obviousness determination in *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945)". See MPEP § 2144.07.

10. Claims 1-6, 8-9 and 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over US5,674,711 in view of US2003144189, US6,632,637, US 6,136,536, US20030083242, US6,852,510 as applied to claims 1-3, 5-6, 8-9 and 11-15 above, and further in view of Logan et al. (Proc. Natl. Acad. Sci. USA, 1984, 81:3655-3659) and WO03/048366.

Claims 1-6, 8-9 and 11-15 are drawn to an expression vector, a transformant and a method of making human FSH protein wherein the expression vector comprises a gene coding human FSH (SEQ ID NOs 1-2 in claim 2), a promoter sequence (SEQ ID NO:8 in claim 3), a polyadenylation motif sequence (SEQ ID NO:13 for SV40 polyA, SEQ ID NO:14 for BGH in claim 5) and a DHFR gene (SEQ ID NO:12 in claim 6) and optionally comprises IRES (SEQ ID NO:7 in claim 2) and tripartite leader sequence of adenovirus (SEQ ID NO:9 in claim 4).

US2003144189, US 6,632,637, US 6,136,536, US20030083242, US 6,852,510 are as set forth above at paragraph 9 but fail to teach an additional adenovirus tripartite leader sequence in the expression vector, and fails to teach SEQ ID NO:9 for tripartite leader sequence of adenovirus (claim 4).

Logan et al. teach that an adenovirus tripartite leader sequence can enhance translation of mRNA (see p. 3655, abstract; p. 3656, 2nd col., 4th paragraph, in particular). WO03/048366 teaches that the adenovirus tripartite leader sequence of the

Logan reference has 100% identity to instant SEQ ID NO:9 as recited in instant claim 4 (see sequence search results and alignment).

It would also have been obvious to one of ordinary skill in the art at the time the instant invention was made to include an adenovirus tripartite leader sequence into an expression vector of the '637 patent comprising an a CMV promoter, an IRES, a DHFR gene, a SV40 polyA sequence and a BGH polyA sequenc to express both human FSH alpha and beta subunits in one vector as recited in the instant claim 2 to generate the human FSH of the '711 patent. The person of ordinary skill in the art would have been motivated to do so with an expectation of success because an adenovirus tripartite leader sequence has been shown to enhance mRNA translation and the expression vector of the '637 patent comprising an a CMV promoter, an IRES, a DHFR gene, a SV40 polyA sequence and a BGH polyA sequence has been successfully used to express two exogenous genes and human FSH functions as a dimer containing FSH alpha and beta subunits. Note that

"The selection of a known material based on its suitability for its intended use supported a prima facie obviousness determination in *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945)". See MPEP § 2144.07.

The sequence search results disclose as follows:

SEQ ID NO:1

```
ADI16433
ID   ADI16433 standard; DNA; 351 BP.
AC   ADI16433;
DT   06-MAY-2004  (first entry)
DE   DNA encoding the alpha-human follicle stimulating hormone protein.
KW   VEGF-FSH; hormone; growth factor; vascular endothelial growth factor;
     follicle stimulating hormone; fertility; spermatogenesis; egg production;
     vascularization; ovarian tissue; antiinfertility; alpha-hFSH; gene; ds.
OS   Homo sapiens.
FH   Key             Location/Qualifiers
FT   CDS             1. .351
                     /*tag= a
                     /product= "Alpha-human follicle stimulating hormone
                     protein"
PN   US2003144189-A1.
```

```
PD   31-JUL-2003.
PF   09-APR-2002; 2002US-00119427.
PR   31-JAN-2002; 2002US-00062931.
PA   (LUBT/) LUSTRADER J.
     (LOBE/) LOBEL L.
PI   Lustbader J, Lobel L;
DR   WPI; 2003-730836/69.
     P-PSDB; AD116434.
PT   A composition for increasing fertility, egg production or
     spermatogenesis, as well as, for increasing vascularization in ovarian
     tissue, comprises at least one subunit of a hormone or growth factor and
     a half-life-increasing moiety.
PS   Disclosure; Fig 18; 41pp; English.
CC   The invention relates to a novel vascular endothelial growth factor-
     follicle stimulating hormone (VEGF-FSH) compound. The novel compound
     comprises at least one subunit of a hormone or growth factor and a half-
     life-increasing moiety, where the hormone or growth factor subunit and
     the half-life-increasing moiety are covalently bound. The invention
     further relates to: a nucleic acid encoding the polypeptide chain of the
     above composition; a vector comprising the above nucleic acid; a cell
     that comprises the above vector; a method for producing a polypeptide,
     comprising growing the cell cited above under conditions permitting
     expression of the polypeptide encoded by the vector, and recovering the
     expressed polypeptide; increasing a subject's fertility or a subject's
     spermatogenesis or egg production, comprising administering to the
     subject an amount of the above composition effective to enhance the
     subject's fertility or the subject's spermatogenesis or egg production;
     and increasing vascularization in a tissue, optionally ovarian tissue,
     comprising contacting the tissue, optionally the ovarian tissue, with an
     amount of the above composition to increase vascularization in the
     tissue. The novel VEGF-FSH compound has antiinfertility activity. The
     composition and methods are useful in increasing fertility, egg
     production or spermatogenesis in a subject, as well as in increasing
     vascularization in a tissue, particularly in ovarian tissue. This
     polynucleotide sequence represents the DNA encoding the alpha-hFSH
     protein of the invention
SQ   Sequence 351 BP; 92 A; 90 C; 76 G; 93 T; 0 U; 0 Other;

  Query Match             99.5%;  Score 349.4;  DB 10;  Length 351;
  Best Local Similarity   99.7%;  Pred. No. 1.2e-109;
  Matches  350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 ATGGATTACTACAGAAAATATGCAGCTATCTTTCTGGTCACATTGTCGGTCTTCTGCAT 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||| ||||||||
Db          1 ATGGATTACTACAGAAAATATGCAGCTATCTTTCTGGTCACATTGTCGGTCTTCTGCAT 60

Qy         61 GTTCTCCATTCCGCTCCTGATGTGCAGGATTGCCCAGAATGCACGCTACAGGAAAACCCA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GTTCTCCATTCCGCTCCTGATGTGCAGGATTGCCCAGAATGCACGCTACAGGAAAACCCA 120

Qy        121 TTCTTCTCCCCAGCCGGGTGCCCCAATACTTCAGTGCATGGGCTGCTGCTTCTCTAGAGCA 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 TTCTTCTCCCCAGCCGGGTGCCCCAATACTTCAGTGCATGGGCTGCTGCTTCTCTAGAGCA 180

Qy        181 TATCCCACTCCACTAAGGTCCAAGAAGACGATGTTGGTCCAAAAGAACGTCACCTCAGAG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 TATCCCACTCCACTAAGGTCCAAGAAGACGATGTTGGTCCAAAAGAACGTCACCTCAGAG 240

Qy        241 TCCACTTGCTGTGTAGCTAAATCATATAACAGGGTCACAGTAATGGGGGGTTTCAAAGTG 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 TCCACTTGCTGTGTAGCTAAATCATATAACAGGGTCACAGTAATGGGGGGTTTCAAAGTG 300

Qy        301 GAGAACCACACGGCGTGCCACTGCAGTACTTGTTATTATCACAAATCTTAA 351
              |||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 GAGAACCACACGGCGTGCCACTGCAGTACTTGTTATTATCACAAATCTTAA 351
```

SEQ ID NO:2

```
ADI16431
ID   ADI16431 standard; DNA; 390 BP.
AC   ADI16431;
DT   06-MAY-2004  (first entry)
DE   DNA encoding the Beta-human follicle stimulating hormone protein.
KW   VEGF-FSH; hormone; growth factor; vascular endothelial growth factor;
     follicle stimulating hormone; fertility; spermatogenesis; egg production;
     vascularization; ovarian tissue; antiinfertility; Beta-hFSH; gene; ds.
OS   Homo sapiens.
FH   Key             Location/Qualifiers
FT   CDS             1. .390
                     /*tag= a
```

```
                     /product= "Beta-human follicle stimulating hormone
                     protein"
PN   US20031441B9-A1.
PD   31-JUL-2003.
PF   09-APR-2002; 2002US-00119427.
PR   31-JAN-2002; 2002US-00062991.
PA   (LUST/) LUST BADER J.
     (LOWE/) LOWEL L.
PI   Lustbader J, Lobel L;
DR   WPI; 2003-730836/69.
     P-PSDB; AD116432.
PT   A composition for increasing fertility, egg production or
     spermatogenesis, as well as, for increasing vascularization in ovarian
     tissue, comprises at least one subunit of a hormone or growth factor and
     a half-life-increasing moiety.
PS   Disclosure; Fig 1/7; 41pp; English.
CC   The invention relates to a novel vascular endothelial growth factor-
     follicle stimulating hormone (VEGF-FSH) compound. The novel compound
     comprises at least one subunit of a hormone or growth factor and a half-
     life-increasing moiety, where the hormone or growth factor subunit and
     the half-life-increasing moiety are covalently bound. The invention
     further relates to: a nucleic acid encoding the polypeptide chain of the
     above composition; a vector comprising the above nucleic acid; a cell
     that comprises the above vector; a method for producing a polypeptide,
     comprising growing the cell cited above under conditions permitting
     expression of the polypeptide encoded by the vector, and recovering the
     expressed polypeptide; increasing a subject's fertility or a subject's
     spermatogenesis or egg production, comprising administering to the
     subject an amount of the above composition effective to enhance the
     subject's fertility or the subject's spermatogenesis or egg production;
     and increasing vascularization in a tissue, optionally ovarian tissue,
     comprising contacting the tissue, optionally the ovarian tissue, with an
     amount of the above composition to increase vascularization in the
     tissue. The novel VEGF-FSH compound has antiinfertility activity. The
     composition and methods are useful in increasing fertility, egg
     production or spermatogenesis in a subject, as well as in increasing
     vascularization in a tissue, particularly in ovarian tissue. This
     polynucleotide sequence represents the DNA encoding the Beta-hFSH protein
     of the invention
XX
SQ   Sequence 390 BP; 108 A; 95 C; 93 G; 94 T; 0 U; 0 Other;

  Query Match             98.8%;  Score 385.2;  DB 10;  Length 390;
  Best Local Similarity   99.2%;  Pred. No. 8.1e-113;
  Matches  387;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 ATGAAGACACTCCAGTTTTTCTTCCTTTTCTGTTGCTGGAAAGCAATCTGCTGCAATAGC 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 ATGAAGACACTCCAGTTTTTCTTCCTTTTCTGTTGCTGGAAAGCAATCTGCTGCAATAGC 60

Qy         61 TGTGAGCTGACCAACATCACCATTGCAATAGAGAAAGAAGAATGTCGTTTCTGCATAAGC 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TGTGAGCTGACCAACATCACCATTGCAATAGAGAAAGAAGAATGTCGTTTCTGCATAAGC 120

Qy        121 ATCAACACCACTTGGTGTGCTGGCTACTGCTACACCAGGGATCTGGTGTATAAGGACCCA 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 ATCAACACCACTTGGTGTGCTGGCTACTGCTACACCAGGGATCTGGTGTATAAGGACCCA 180

Qy        181 GCCAGGCCCAAAATCCAGAAAACATGTACCTTCAAGGAACTGGTATATGAAACAGTGAGA 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 GCCAGGCCCAAAATCCAGAAAACATGTACCTTCAAGGAACTGGTATATGAAACAGTGAGA 240

Qy        241 GTGCCCGGCTGTGCTCACCATGCAGATTCCTTGTATACATACCCAGTGGCCACCCAGGTG 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 GTGCCCGGCTGTGCTCACCATGCAGATTCCTTGTATACATACCCAGTGGCCACCCAGTGT 300

Qy        301 CACTGTGGCAAGTGTGACAGCGACAGCACTGATTGTACTGTGCGAGGCCTGGGGCCCAGC 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 CACTGTGGCAAGTGTGACAGCGACAGCACTGATTGTACTGTGCGAGGCCTGGGGCCCAGC 360

Qy        361 TACTGCTCCTTTGGTGAAATGAAAGAATAA 390
              |||||||||||||||||||||||||||||
Db        361 TACTGCTCCTTTGGTGAAATGAAAGAATAA 390
```

SEQ ID NO:7 GATATCGAATTC EcoRI site

```
US-09-897-511A-12
; Sequence 12, Application US/09897511A
; Patent No. 6852510
```

```
; GENERAL INFORMATION:
;  APPLICANT: Bremel, Robert
;  APPLICANT:  Miller, Linda
;  APPLICANT:  Bleck, Gregory
;  TITLE OF INVENTION: Host Cells Containing Multiple Integrating Vectors
;  FILE REFERENCE: GAIA-16416
;  CURRENT APPLICATION NUMBER: US/09/897,511A
;  CURRENT FILING DATE:  2001-06-29
;  PRIOR APPLICATION NUMBER: 60/215,925
;  PRIOR FILING DATE: 2000-07-03
;  NUMBER OF SEQ ID NOS: 36
;  SOFTWARE: PatentIn version 3.0
; SEQ ID NO 12
;   LENGTH: 668
;   TYPE: DNA
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Synthetic
US-09-897-511A-12

  Query Match           97.0%;  Score 574.2;  DB 3;  Length 668;
  Best Local Similarity   99.5%;  Pred. No. 1.2e-189;
  Matches  576;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          8 AATTC CCCCCTCCCCTCCCCCCCCCCTAACGTTACTGGCCGAAGCCGCTTGGAATAAGGC 67
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          4 ATTCG CCCCTCTCCCTCCCCCCCCCCTAACGTTACTGGCCGAAGCCGCTTGGAATAAGGC 63

Qy         68 CGGTGTGCGTTTGTCTATATGTTATTTTCCACCATATTGCCGTCTTTTGGCAATGTGAGG 127
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         64 CGGTGTGCGTTTGTCTATATGTTATTTTCCACCATATTGCCGTCTTTTGGCAATGTGAGG 123

Qy        128 GCCCGGAAACCTGGCCCTGTCTTCTTGACGAGCATTCCTAGGGGTCTTTCCCCTCTCGCC 187
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        124 GCCCGGAAACCTGGCCCTGTCTTCTTGACGAGCATTCCTAGGGGTCTTTCCCCTCTCGCC 183

Qy        188 AAAGGAATGCAAGGTCTGTTGAATGTCGTGAAGGAAGCAGTTCCTCTGGAAGCTTCTTGA 247
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        184 AAAGGAATGCAAGGTCTGTTGAATGTCGTGAAGGAAGCAGTTCCTCTGGAAGCTTCTTGA 243

Qy        248 AGACAAACAACGTCTGTAGCGACCCTTTGCAGGCAGCGGAACCCCCCACCTGGCGACAGG 307
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        244 AGACAAACAACGTCTGTAGCGACCCTTTGCAGGCAGCGGAACCCCCACCTGGCGACAGG 303

Qy        308 TGCCTCTGCGGCCAAAAGCCACGTGTATAAGATACACCTGCAAAGGCGGCACAACCCCAG 367
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        304 TGCCTCTGCGGCCAAAAGCCACGTGTATAAGATACACCTGCAAAGGCGGCACAACCCCAG 363

Qy        368 TGCCACGTTGTGAGTTGGATAGTTGTGGAAAGAGTCAAATGGCTCTCCTCAAGCGTATTC 427
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        364 TGCCACGTTGTGAGTTGGATAGTTGTGGAAAGAGTCAAATGGCTCTCCTCAAGCGTATTC 423

Qy        428 AACAAGGGGCTGAAGGATGCCCAGAAGGTACCCCATTGTATGGGATCTGATCTGGGGCCT 487
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        424 AACAAGGGGCTGAAGGATGCCCAGAAGGTACCCCATTGTATGGGATCTGATCTGGGGCCT 483

Qy        488 CGGTGCACATGCTTTACATGTGTTTAGTCGAGGTTAAAAAAACGTCTAGGCCCCCCGAAC 547
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        484 CGGTGCACATGCTTTACATGTGTTTAGTCGAGGTTAAAAAAACGTCTAGGCCCCCCGAAC 543

Qy        548 CACGGGGACGTGGTTTTCCTTTGAAAAACACGATGATAA 586
              |||||||||||||||||||||||||||||||||||||||
Db        544 CACGGGGACGTGGTTTTCCTTTGAAAAACACGATGATAA 582
```

SEQ ID NO:8

```
AAA30286
US-09-187-387-25
; Sequence 25, Application US/09187387
; Publication No. US20030083242A1
; GENERAL INFORMATION:
;  APPLICANT: Galdes, Alphonse
;  APPLICANT: Mahanthappa, Nagesh
;  TITLE OF INVENTION: METHODS AND COMPOSITIONS FOR TREATING OR PREVENTING
;  TITLE OF INVENTION: PERIPHERAL NEUROPATHIES
;  FILE REFERENCE: ONV-052.01
;  CURRENT APPLICATION NUMBER: US/09/187,387
;  CURRENT FILING DATE: 1998-11-06
;  NUMBER OF SEQ ID NOS: 28
;  SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 25
;   LENGTH: 996
```

```
;   TYPE: DNA
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Description of Artificial Sequence: gene
;   OTHER INFORMATION: activation construct
US-09-187-787-2:

  Query Match             99.3%;  Score 649.2;  DB 3;  Length 996;
  Best Local Similarity   99.5%;  Pred. No. 2.5e-194;
  Matches  651;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 GATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTATTAATAGTAATCA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        239 GATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTATTAATAGTAATCA 298

Qy         61 ATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        299 ATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTA 358

Qy        121 AATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTAT 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        359 AATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTAT 418

Qy        181 GTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGACTATTTACGG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        419 GTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGACTATTTACGG 478

Qy        241 TAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGAC 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        479 TAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGAC 538

Qy        301 GTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTT 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        539 GTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTT 598

Qy        361 CCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGG 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        599 CCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGG 658

Qy        421 CAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCC 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        659 CAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCC 718

Qy        481 ATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGT 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        719 ATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGT 778

Qy        541 AACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATA 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        779 AACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATA 838

Qy        601 AGCAGAGCTCTCTGGCTAACTAGAGAACCCACTGCTTA[ACT]GCTTATCGAAATT 654
              ||||||||||||||||||||||||||||||||||||| |||||||||||||||||||
Db        839 AGCAGAGCTCTCTGGCTAACTAGAGAACCCACTGCTTA[CTG]CTTATCGAAATT 892
```

SEQ ID NO:9

```
ACC84842
ID   ACC84842 standard; DNA; 3641 BP.
AC   ACC84842;
DT   12-SEP-2003  (first entry)
DE   Nucleotide sequence of vector sequence Id NO. 60.
KW   pGX10; anti-HIV; vaccine; AIDS; ds.
OS   Synthetic.
PN   WO2003068966-A1.
PD   12-JUN-2003.
PF   08-MAY-2002; 2002WO-KR000855.
PR   07-DEC-2001; 2001KR-00079870.
     30-APR-2002; 2002KR-00023839.
PA   (POST-) POSTECH FOUND.
     (GENE-) GENEKINE CO LTD.
PI   Sung Y, Suh Y;
DR   WPI; 2003-513765/48.
PT   New pGX10 vector, useful for preparing a composition for preventing or
     treating AIDS.
PS   Example; Page 191-194; 196pp; English.
CC   The invention relates to a new pGX10 vector. The vector is useful for
     preparing a vaccine for preventing or treating AIDS. The present sequence
     represents a vector constructed during the course of the invention
SQ   Sequence 3641 BP; 845 A; 968 C; 962 G; 866 T; 0 U; 0 Other;
```

```
  Query Match           100.0%;  Score 441;  DB 9;  Length 3641;
  Best Local Similarity   100.0%;  Pred. No. 3.4e-126;
  Matches  441;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 TCGATACTCTCTTTCCGCATCGCTGTCTGCGAGGGCCAGCTGTTGGGCTTCGCGGTTGAGCA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        666 TCGATACTCTCTTTCCGCATCGCTGTCTGCGAGGGCCAGCTGTTGGGCTTCGCGGTTGAGCA 725

Qy         61 CAAACTCTTCGCGGTCTTTCCAGTACTCTTGGATCGGAAACCCGTCGGCCTCCGAACGGT 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        726 CAAACTCTTCGCGGTCTTTCCAGTACTCTTGGATCGGAAACCCGTCGGCCTCCGAACGGT 785

Qy        121 ACTCCGCCACCGAGGGACCTGAGCGAGTCCGCATCGACCGGATCGGAAAACCTCTCGACT 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        786 ACTCCGCCACCGAGGGACCTGAGCGAGTCCGCATCGACCGGATCGGAAAACCTCTCGACT 845

Qy        181 GTTGGGGTGAGTACTCCCTCTCAAAAGCGGGCATGACTTCTGCGCTAAGATTGTCAGTTT 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        846 GTTGGGGTGAGTACTCCCTCTCAAAAGCGGGCATGACTTCTGCGCTAAGATTGTCAGTTT 905

Qy        241 CCAAAAACGAGGAGGATTTGATATTCACCTGGCCCGCGGTGATGCCTTTGAGGGTGGCCG 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        906 CCAAAAACGAGGAGGATTTGATATTCACCTGGCCCGCGGTGATGCCTTTGAGGGTGGCCG 965

Qy        301 CGTCCATCTGGTCAGAAAAGACAATCTTTTTGTTGTCAAGCTTGAGGTGTGGCAGGCTTG 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        966 CGTCCATCTGGTCAGAAAAGACAATCTTTTTGTTGTCAAGCTTGAGGTGTGGCAGGCTTG 1025

Qy        361 AGATCTGGCCATACACTTGAGTGACAATGACATCCACTTTGCCTTTCTCTCCACAGGTGT 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1026 AGATCTGGCCATACACTTGAGTGACAATGACATCCACTTTGCCTTTCTCTCCACAGGTGT 1085

Qy        421 CCACTCCCAGGTCCAACTGCA 441
              |||||||||||||||||||||
Db       1086 CCACTCCCAGGTCCAACTGCA 1106
```

SEQ ID NO:14

```
US-09-687-050-2
; Sequence 2, Application US/09687050
; Patent No. 6632637
; GENERAL INFORMATION:
;  APPLICANT:  McGrew, Jeffrey T.
;  TITLE OF INVENTION:  VECTORS AND METHODS FOR RECOMBINANT PROTEIN EXPRESSION
;  FILE REFERENCE:  2902-A
;  CURRENT APPLICATION NUMBER:  US/09/687,050
;  CURRENT FILING DATE:  2000-10-12
;  PRIOR APPLICATION NUMBER:  60/159,177
;  PRIOR FILING DATE:  1999-10-13
;  NUMBER OF SEQ ID NOS:  10
;  SOFTWARE:  PatentIn version 3.0
; SEQ ID NO 2
;  LENGTH: 285
;  TYPE: DNA
;  ORGANISM: Bovine
US-09-687-050-2

  Query Match           100.0%;  Score 232;  DB 3;  Length 285;
  Best Local Similarity   100.0%;  Pred. No. 2.6e-69;
  Matches  232;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CTAGAGCTCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCC 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          7 CTAGAGCTCGCTGATCAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCC 66

Qy         61 CCTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         67 CCTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAA 126

Qy        121 ATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGGTGG 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        127 ATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGGTGG 186

Qy        181 GGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCATGCTGGGGA 232
              ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        187 GGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCATGCTGGGGA 238
```

Conclusion

11. NO CLAIM IS ALLOWED.

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

SEQ ID NO:1

```
AAV02211
ID   AAV02211 standard; DNA; 351 BP.
AC   AAV02211;
DT   27-MAR-1998  (first entry)
DE   Secreted protein human chorionic gonadotropin (HCG alpha) encoding DNA.
KW   leaderless protein; inhibitor; cardiac glycoside; aglycone; treatment;
KW   carcinoma; diabetes; secreted protein; human chorionic gonadotropin;
KW   HCG alpha; ss.
OS   Homo sapiens.
FH   Key             Location/Qualifiers
FT   CDS             1. .351
FT                   /*tag= a
PN   WO9728808-A1.
PD   14-AUG-1997.
PF   12-FEB-1997;   97WO-US002237.
PR   12-FEB-1996;   96US-0599895.
PA   (SCRI ) SCRIPPS RES INST.
PI   Florkiewicz RZ;
DR   WPI; 1997-415065/38.
DR   P-PSDB; AAW31665.
PT   Inhibition of export of leaderless protein from cells - using cardiac
PT   glycoside or its aglycone, e.g. ouabain or digoxin.
PS   Disclosure; Page 28; 61pp; English.
CC   This DNA encodes for the secreted protein human chorionic gonadotropin
CC   (HCG alpha). These proteins are exported in the cell by means of a leader
CC   sequence. The export of leaderless proteins from a cell can be inhibited
CC   by a method which comprises contacting the cell with a cardiac glycoside
CC   or with an aglycone derivative of a cardiac glycoside. Such a method
CC   should not interfere in the export of secreted proteins with a leader
CC   sequence like HCG alpha. Preferably the glycoside in the method is
CC   digoxin, strophanthin K, digitoxin, lanatoside A, ouabain, gitoxin,
CC   oleandrin or acovenoside A, and the aglycone is strophanthidin,
CC   digoxigenin, digitoxigenin or uzarigenin. The method is useful for
CC   inhibiting export of leaderless proteins like FGF-1, FGF-2, IL-1 alpha,
CC   IL-1 beta , PD-ECGF, CNTF, thymosin, parathymosin, factor XIIIa, vas
CC   deferens protein, sciatic nerve growth promoting protein, L-14 lectin,
CC   transglutaminase, thioredoxin-like protein, HIV tat and int-2. Inhibition
CC   of export of FGF is useful for treating FGF-mediated pathophysiological
CC   conditions (e.g. melanoma, ovarian carcinoma, teratocarcinoma and
CC   neuroblastoma), It is useful for inhibiting proliferation of cells
CC   bearing an FGF-receptor, and for treating complications of diabetes
SQ   Sequence 351 BP; 92 A; 90 C; 76 G; 93 T; 0 U; 0 Other;

  Query Match             99.5%;  Score 349.4;  DB 2;  Length 351;
  Best Local Similarity   99.7%;  Pred. No. 1.2e-109;
  Matches  350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 ATGGATTACTACAGAAAATATGCAGCTATCTTTCTGGTCACATTGTCGGTCTTTCTGCAT 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 ATGGATTACTACAGAAAATATGCAGCTATCTTTCTGGTCACATTGTCGGTCTTTCTGCAT 60

Qy         61 GTTCTCCATTCCGCTCCTGATGTGCAGGATGCCCAGAATGCACGCTACAGGAAAACCCA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
```

```
Db         61 GTTCTCCATTCCGCTCCTGATGTGCAGGATTGCCCAGAATGCACGCTACAGGAAAACCCA 120

Qy        121 TTCTTCTCCCAGCCGGGTGCCCCAATACTTCAGTGCATGGGCTGCTGCTTCTCTAGAGCA 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 TTCTTCTCCCAGCCGGGTGCCCCAATACTTCAGTGCATGGGCTGCTGCTTCTCTAGAGCA 180

Qy        181 TATCCCACTCCACTAAGGTCCAAGAAGACGATGTTGGTCCAAAAGAACGTCACCTCAGAG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 TATCCCACTCCACTAAGGTCCAAGAAGACGATGTTGGTCCAAAAGAACGTCACCTCAGAG 240

Qy        241 TCCACTTGCTGTGTAGCTAAATCATATAACAGGGTCACAGTAATGGGGGGTTTCAAAGTG 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 TCCACTTGCTGTGTAGCTAAATCATATAACAGGGTCACAGTAATGGGGGGTTTCAAAGTG 300

Qy        301 GAGAACCACACGGCGTGCCACTGCAGTACTTGTTATTATCACAAATCTTAA 351
              |||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 GAGAACCACACGGCGTGCCACTGCAGTACTTGTTATTATCACAAATCTTAA 351


AAA53565
ID   AAA53565 standard; cDNA; 351 BP.
AC   AAA53565;
DT   31-OCT-2000  (first entry)
DE   Human chorionic gonadotropin alpha cDNA.
KW   hCG-alpha; chorionic gonadotropin; transport molecule; leaderless;
KW   Endoplasmic reticulum; golgi; protein export; detection; inhibitor; ss.
OS   Homo sapiens.
FH   Key             Location/Qualifiers
FT   CDS             1..351
FT                   /*tag= a
FT                   /product= "Chorionic_gonadotrophin_alpha"
PN   US6083706-A.
PD   04-JUL-2000.
PF   25-FEB-1998;   98US-00030613.
PR   26-FEB-1997;   97US-00807014.
PA   (CIBA-) CIBLEX CORP.
PI   Baird A,  Florkiewicz RZ;
DR   WPI; 2000-464338/40.
DR   P-PSDB; AAY96874.
PT   Detecting transport molecules, useful for identifying proteins that
PT   mediate leaderless protein export across cell membranes, by contacting
PT   cell extracts with a fusion protein of leaderless protein and a tag to
PT   form a complex.
PS   Example 4; Col 37-38; 64pp; English.
XX
CC   Human chorionic gonadotropin-alpha is secreted into cellular medium and
CC   is brefeldin sensitive and energy dependent. hCG-alpha contains a
CC   hydrophobic leader (signal) sequence and as a consequence is secreted via
CC   the endoplasmic reticulum (ER) and golgi. Detecting a transport molecule
CC   involved in non-ER/Golgi leaderless protein export, comprises contacting
CC   test cell extracts or membranes with a fusion protein of a leaderless
CC   protein and a tag to form a complex of the fusion protein bound to the
CC   transport molecule, and detecting the transport molecule in an isolated
CC   complex. The leaderless protein is a protein found in the extracellular
CC   environment that lacks a canonical leader sequence, interleukin (IL) 1-
CC   alpha,or 1-beta, fibroblast growth factor (FGF) 1 or 2, human
CC   immunodeficiency virus (HIV) tat, platelet-derived endothelial cell
CC   growth factor (PD-ECGF), ciliary neurotrophic factor (CNTF), sciatic
CC   nerve growth-promoting activity, vas deferens protein, transglutaminase,
CC   L-14 lectin, factor XIIIa, thioredoxin-like protein (ADF), thymosin,
CC   parathymosin, mammary-derived growth inhibitor, galectin or rhodanase.
CC   The method is used to detect proteins, complexes of proteins, or parts of
CC   a larger complex, that bind to and mediate the transport of leaderless
CC   proteins, e.g. Na+/K+ ATPase which is an integral membrane protein
CC   responsible for transporting sodium and potassium ions across the cell
CC   membrane using ATP as the driving force. Transport molecules detected by
CC   the method are used in assays to identify inhibitors of the interaction
CC   with a leaderless protein
SQ   Sequence 351 BP; 92 A; 90 C; 76 G; 93 T; 0 U; 0 Other;

  Query Match          99.5%;  Score 349.4;  DB 3;  Length 351;
  Best Local Similarity   99.7%;  Pred. No. 1.2e-109;
  Matches  350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 ATGGATTACTACAGAAAATATGCAGCTATCTTTCTGGTCACATTGTCGGTCTTTCTGCAT 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||| ||||||||
Db          1 ATGGATTACTACAGAAAATATGCAGCTATCTTTCTGGTCACATTGTCGGTGTTTCTGCAT 60

Qy         61 GTTCTCCATTCCGCTCCTGATGTGCAGGATTGCCCAGAATGCACGCTACAGGAAAACCCA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GTTCTCCATTCCGCTCCTGATGTGCAGGATTGCCCAGAATGCACGCTACAGGAAAACCCA 120

Qy        121 TTCTTCTCCCAGCCGGGTGCCCCAATACTTCAGTGCATGGGCTGCTGCTTCTCTAGAGCA 180
```

```
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 TTCTTCTCCCAGCCGGGTGCCCCAATACTTCAGTGCATGGGCYGCTGCTTCTCTAGAGCA 180

Qy        181 TATCCCACTCCACTAAGGTCCAAGAAGACGATGTTGGTCCAAAAGAACGTCACCTCAGAG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 TATCCCACTCCACTAAGGTCCAAGAAGACGATGTTGGTCCAAAAGAACGTCACCTCAGAG 240

Qy        241 TCCACTTGCTGTGTAGCTAAATCATATAACAGGGTCACAGTAATGGGGGGTTTCAAAGTG 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 TCCACTTGCTGTGTAGCTAAATCATATAACAGGGTCACAGTAATGGGGGGTTTCAAAGTG 300

Qy        301 GAGAACCACACGGCGTGCCACTGCAGTACTTGTTATTATCACAAATCTTAA 351
              |||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 GAGAACCACACGGCGTGCCACTGCAGTACTTGTTATTATCACAAATCTTAA 351


AD116433
ID   AD116433 standard; DNA; 351 BP.
AC   AD116433;
DT   06-MAY-2004  (first entry)
DE   DNA encoding the alpha-human follicle stimulating hormone protein.
KW   VEGF-PSH; hormone; growth factor; vascular endothelial growth factor;
KW   follicle stimulating hormone; fertility; spermatogenesis; egg production;
KW   vascularization; ovarian tissue; antiinfertility; alpha-hPSH; gene; ds.
OS   Homo sapiens.
FH   Key             Location/Qualifiers
FT   CDS             1. .351
FT                   /*tag= a
FT                   /product= "Alpha-human follicle stimulating hormone
FT                   protein"
PN   US20033144189-A1.
PD   31-JUL-2003.
PF   09-APR-2002; 2002US-00119427.
PR   31-JAN-2002; 2002US-00062931.
PA   (LUST/) LUSTBADER J.
PA   (LOBE/) LOBEL L.
PI   Lustbader J,  Lobel L;
DR   WPI; 2003-730836/69.
DR   P-PSDB; AD116434.
PT   A composition for increasing fertility, egg production or
PT   spermatogenesis, as well as, for increasing vascularization in ovarian
PT   tissue, comprises at least one subunit of a hormone or growth factor and
PT   a half-life-increasing moiety.
PS   Disclosure; Fig 18; 41pp; English.
CC   The invention relates to a novel vascular endothelial growth factor-
CC   follicle stimulating hormone (VEGF-FSH) compound. The novel compound
CC   comprises at least one subunit of a hormone or growth factor and a half-
CC   life-increasing moiety, where the hormone or growth factor subunit and
CC   the half-life-increasing moiety are covalently bound. The invention
CC   further relates to: a nucleic acid encoding the polypeptide chain of the
CC   above composition; a vector comprising the above nucleic acid; a cell
CC   that comprises the above vector; a method for producing a polypeptide,
CC   comprising growing the cell cited above under conditions permitting
CC   expression of the polypeptide encoded by the vector, and recovering the
CC   expressed polypeptide; increasing a subject's fertility or a subject's
CC   spermatogenesis or egg production, comprising administering to the
CC   subject an amount of the above composition effective to enhance the
CC   subject's fertility or the subject's spermatogenesis or egg production;
CC   and increasing vascularization in a tissue, optionally ovarian tissue,
CC   comprising contacting the tissue, optionally the ovarian tissue, with an
CC   amount of the above composition to increase vascularization in the
CC   tissue. The novel VEGF-PSH compound has antiinfertility activity. The
CC   composition and methods are useful in increasing fertility, egg
CC   production or spermatogenesis in a subject, as well as in increasing
CC   vascularization in a tissue, particularly in ovarian tissue. This
CC   polynucleotide sequence represents the DNA encoding the alpha-hPSH
CC   protein of the invention
SQ   Sequence 351 BP; 92 A; 90 C; 76 G; 93 T; 0 U; 0 Other;

  Query Match             99.5%;  Score 349.4;  DB 10;  Length 351;
  Best Local Similarity   99.7%;  Pred. No. 1.2e-109;
  Matches  350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 ATGGATTACTACAGAAAATATGCAGCTATCTTTCTGGTCACATTGTCGGTCTTTCTGCAT 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||| |||||||||
Db          1 ATGGATTACTACAGAAAATATGCAGCTATCTTTCTGGTCACATTGTCGGTGTTTCTGCAT 60

Qy         61 GTTCTCCATTCCGCTCCTGATGTGCAGGATTGCCCAGAATGCACGCTACAGGAAAACCA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GTTCTCCATTCCGCTCCTGATGTGCAGGATTGCCCAGAATGCACGCTACAGGAAAACCA 120

Qy        121 TTCTTCTCCCAGCCGGGTGCCCCAATACTTCAGTGCATGGGCYGCTGCTTCTCTAGAGCA 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
```

```
Db        121 TTCCTCCCCAGCCGGGTGCCCAATACTTCAGTGCATGGGCTGCTGCTTCTCTAGAGCA 180

Qy        181 TATCCCACTCCACTAAGGTCCAAGAAGACGATGTTGGTCCAAAAGAACGTCACCTCAGAG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 TATCCCACTCCACTAAGGTCCAAGAAGACGATGTTGGTCCAAAAGAACGTCACCTCAGAG 240

Qy        241 TCCACTTGCTGTGTAGCTAAATCATATAACAGGGTCACAGTAATGGGGGGTTTCAAAGTG 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 TCCACTTGCTGTGTAGCTAAATCATATAACAGGGTCACAGTAATGGGGGGTTTCAAAGTG 300

Qy        301 GAGAACCACACGGCGTGCCACTGCAGTACTTGTTATTATCACAAATCTTAA 351
              |||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 GAGAACCACACGGCGTGCCACTGCAGTACTTGTTATTATCACAAATCTTAA 351
```

SEQ ID NO:8

```
ID   AAA30286 standard; DNA; 996 BP.
AC   AAA30286;
DT   11-SEP-2000  (first entry)
DE   Human Shh gene and CMV promoter construct.
KW   Human; sonic hedgehog; Shh; neuromuscular disorder; neuropathy;
KW   Guillain-Barre syndrome; peripheral neuropathy; diabetes; alcoholism;
KW   chronic inflammatory demyelinating polyneuropathy; CIPD; gene therapy;
KW   infection; inflamation; hereditary neuropathy;
KW   Charcot-Marie-Tooth disease; vasculitis; lung cancer; tumour;
KW   multiple myeloma; nutritional imbalance; kidney disease;
KW   hypothyroid neuropathy; trauma; Refsum's disease; Abetalipoproteinemia;
KW   Tangier disease; Krabbe's disease; Metachromatic leukodystrophy;
KW   Fabry's disease; CMT; GBS; Dejerine-Sottas syndrome; acute neuropathy;
KW   Amyotrophic lateral sclerosis; ALS; Miller-Fisher syndrome; amylodosis;
KW   Hereditary sensory neuropathy Type II; HSN II; B-cell lymphoma;
KW   Waldenstrom's Macroglobulaemia; Chronic Lymphocytic Leukaemia;
KW   neuroprotective; cytoprotective; cytomegalovirus promoter; CMV promoter;
KW   patched-mediated signal transduction; ds.
OS   Homo sapiens.
PN   WO2000027422-A2.
PD   18-MAY-2000.
PF   08-NOV-1999;   99WO-US026334.
PR   06-NOV-1998;   98US-00187387.
PA   (BIOG ) BIOGEN INC.
PA   (GNTO-) GENTHERAY INC.
PI   Galdes A,  Mahanthappa N;
DR   WPI; 2000-387341/33.
PT   Novel method of preventing deterioration of peripheral nerves, useful for
PT   treating or preventing neuropathy, e.g. where associated with diabetes or
PT   viral infection, by administering hedgehog or patched agent.
PS   Disclosure; Page 50-51; 152pp; English.
CC   The present sequence is a human Sonic hedgehog gene, Shh and
CC   cytomegalovirus, CMV promoter construct. This gene fragment can then be
CC   inserted into a vector, e.g. pCDNA1.1. This recombinant vector may then
CC   be used in gene therapy of various neuromuscular disorders (neuropathies)
CC   i.e. preventing degradation in function of motor or sensory nerves and
CC   protecting peripheral nerve cells under conditions that normally cause
CC   neuropathy since the hedgehog gene inhibits expression of the patched
CC   gene. The patched gene is implicated in neuropathies. A variety of
CC   neuromuscular disorders may be treated: Guillain-Barre syndrome, GBS;
CC   peripheral neuropathy; diabetic neuropathy; alcohol-induced neuropathy;
CC   chronic inflammatory demyelinating polyneuropathy, CIPD; infection-
CC   induced neuropathy, including HIV infection; inflammation-induced
CC   neuropathy; hereditary neuropathy e.g. Charcot-Marie-Tooth disease (CMT),
CC   Familial Amyloidotic neuropathy, Refsum's disease, Abetalipoproteinemia,
CC   Tangier disease, Krabbe's disease, Metachromatic leukodystrophy, Fabry's
CC   disease, Dejerine-Sottas syndrome, Hereditary sensory neuropathy Type II
CC   (HSN II) and Amyotrophic lateral sclerosis (ALS); acute neuropathy e.g
CC   Miller-Fisher syndrome; neuropathy caused by vasculitis; neuropathy
CC   associated with tumours e.g. lung cancer, multiple myeloma, B-cell
CC   lymphoma, Waldenstrom's Macroglobulaemia, Chronic Lymphocytic Leukaemia;
CC   neuropathy associated with: amylodosis, nutritional imbalance, kidney
CC   disease, trauma; and hypothyroid neuropathy
SQ   Sequence 996 BP; 257 A; 248 C; 255 G; 236 T; 0 U; 0 Other;

  Query Match             99.3%;  Score 649.2;  DB 3;  Length 996;
  Best Local Similarity   99.5%;  Pred. No. 1.2e-196;
  Matches  651;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 GATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTATTAATAGTAATCA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        239 GATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTATTAATAGTAATCA 298

Qy         61 ATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        299 ATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTA 358
```

```
Qy       121 AATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTAT 180
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       359 AATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTAT 418

Qy       181 GTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGACTATTTACGG 240
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       419 GTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGACTATTTACGG 478

Qy       241 TAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGAC 300
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       479 TAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGAC 538

Qy       301 GTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTT 360
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       539 GTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTT 598

Qy       361 CCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGG 420
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       599 CCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGG 658

Qy       421 CAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCC 480
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       659 CAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCC 718

Qy       481 ATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGT 540
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       719 ATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGT 778

Qy       541 AACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATA 600
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       779 AACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATA 838

Qy       601 AGCAGAGCTCTCTGGCTAACTAGAGAACCCACTGCTTAACTGCTTATCGAAATT 654
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       839 AGCAGAGCTCTCTGGCTAACTAGAGAACCCACTGCTTACTGGCTTATCGAAATT 892


US-09-418-221-23
; Sequence 23, Application US/09418221
; Patent No. 6767888
; GENERAL INFORMATION:
;  APPLICANT: Mahanthappa, Nagesh K.
;  TITLE OF INVENTION: NEUROPROTECTIVE METHODS AND REAGENTS
;  FILE REFERENCE: ONV-043.02
;  CURRENT APPLICATION NUMBER: US/09/418,221
;  CURRENT FILING DATE: 1999-10-14
;  EARLIER APPLICATION NUMBER: 08/883,656
;  EARLIER FILING DATE: 1997-06-27
;  NUMBER OF SEQ ID NOS: 26
;  SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 23
;   LENGTH: 996
;   TYPE: DNA
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Description of Artificial Sequence: gene
;   OTHER INFORMATION: activation construct
US-09-418-221-23

  Query Match          99.3%;  Score 649.2;  DB 3;  Length 996;
  Best Local Similarity   99.5%;  Pred. No. 3.5e-199;
  Matches  651;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy         1 GATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTATTAATAGTAATCA 60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       239 GATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTATTAATAGTAATCA 298

Qy        61 ATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTA 120
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       299 ATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTA 358

Qy       121 AATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTAT 180
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       359 AATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTAT 418

Qy       181 GTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGACTATTTACGG 240
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       419 GTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGACTATTTACGG 478

Qy       241 TAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGAC 300
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       479 TAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGAC 538
```

```
Qy        301 GTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTT 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        539 GTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTT 598

Qy        361 CCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGG 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        599 CCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGG 658

Qy        421 CAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCC 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        659 CAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCC 718

Qy        481 ATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGT 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        719 ATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGT 778

Qy        541 AACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATA 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        779 AACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATA 838

Qy        601 AGCAGAGCTCTCTGGCTAACTAGAGAACCCACTGCTTACTGCTTATCGAAATT 654
              |||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        839 AGCAGAGCTCTCTGGCTAACTAGAGAACCCACTGCTTACTGGCTTATCGAAATT 892
```

SEQ ID NO:12

```
AAD42468
ID   AAD42468 standard; DNA; 5155 BP.
AC   AAD42468;
DT   15-NOV-2002  (first entry)
DE   Human plasmid pXMT3 encoding dihydrofolate reductase.
KW   Human; vanilloid receptor; noxious stimulus; pain; receptor; plasmid; ds.
OS   Homo sapiens.
PN   US6406908-A1.
PD   18-JUN-2002.
PF   23-MAR-2000; 2000US-00533220.
PR   26-MAR-1999;  99GB-00007097.
PA   (NOVS ) NOVARTIS AG.
PI   Mcintyre P,  James IF;
DR   WPI; 2002-581941/62.
PT   Novel isolated nucleic acid encoding human vanilloid receptor that is
PT   useful for detecting noxious stimuli in mammalian organisms, and in
PT   assays for testing compounds for their potential to decrease pain in
PT   humans.
PS   Example A1; Col 17-22; 14pp; English.
CC   The invention relates to an isolated nucleic acid encoding a human
CC   vanilloid receptor. The human vanilloid receptor is useful for detecting
CC   noxious stimuli in mammalian organisms, and in assays for testing
CC   compounds for their potential to decrease pain in humans. The present
CC   sequence is human plasmid pXMT3 encoding dihydrofolate reductase
SQ   Sequence 5155 BP; 1245 A; 1278 C; 1395 G; 1237 T; 0 U; 0 Other;

  Query Match           100.0%;  Score 564;  DB 6;  Length 5155;
  Best Local Similarity  100.0%;  Pred. No. 7.6e-166;
  Matches  564;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 ATGGTTCGACCATTGAACTGCATCGTCGCCGTGTCCCAAAATATGGGGATTGGCAAGAAC 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1197 ATGGTTCGACCATTGAACTGCATCGTCGCCGTGTCCCAAAATATGGGGATTGGCAAGAAC 1256

Qy         61 GGAGACCTACCCTGGCCTCCGCTCAGGAACGAGTTCAAGTACTTCCAAAGAATGACCACA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1257 GGAGACCTACCCTGGCCTCCGCTCAGGAACGAGTTCAAGTACTTCCAAAGAATGACCACA 1316

Qy        121 ACCTCTTCAGTGGAAGGTAAACAGAATCTGGTGATTATGGGTAGGAAAACCTGGTTCTCC 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1317 ACCTCTTCAGTGGAAGGTAAACAGAATCTGGTGATTATGGGTAGGAAAACCTGGTTCTCC 1376

Qy        181 ATTCCTGAGAAGAATCGACCTTAAAGGACAGAATTAATATAGTTCTCAGTAGAGAACTC 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1377 ATTCCTGAGAAGAATCGACCTTAAAGGACAGAATTAATATAGTTCTCAGTAGAGAACTC 1436

Qy        241 AAAGAACCACCACGAGGAGCTCATTTCTTGCCAAAAGTTTGGATGATGCCTTAAGACTT 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1437 AAAGAACCACCACGAGGAGCTCATTTCTTGCCAAAAGTTTGGATGATGCCTTAAGACTT 1496

Qy        301 ATTGAACAACCGGAATTGGCAAGTAAAGTAGACATGGTTTGGATAGTCGGAGGCAGTTCT 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1497 ATTGAACAACCGGAATTGGCAAGTAAAGTAGACATGGTTTGGATAGTCGGAGGCAGTTCT 1556

Qy        361 GTTTACCAGGAAGCCATGAATCAACCAGGCCACCTCAGACTCTTTGTGACAAGGATCATG 420
```

```
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1557 GTTACCAGGAAGCCATGAATCAACCAGGCCACCTCAGACTCTTTGTGACAAGGATCATG 1616

Qy        421 CAGGAATTTGAAAGTGACACGTTTTTCCCAGAAATTGATTTGGGGAAATATAAACTTCTC 480
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1617 CAGGAATTTGAAAGTGACACGTTTTTCCCAGAAATTGATTTGGGGAAATATAAACTTCTC 1676

Qy        481 CCAGAATACCCAGCGTCCTCTCTGAGGTCCAGGAGGAAAAAGGCATCAAGTATAAGTTT 540
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1677 CCAGAATACCCAGCGTCCTCTCTGAGGTCCAGGAGGAAAAAGGCATCAAGTATAAGTTT 1736

Qy        541 GAAGTCTACGAGAAGAAAGACTAA 564
                ||||||||||||||||||||||||
Db       1737 GAAGTCTACGAGAAGAAAGACTAA 1760
```

13. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
June 9, 2008

/Jeffrey Stucker/
Supervisory Patent Examiner, Art Unit 1649